# Preface

Corrosive substances are defined as chemicals that cause visible destruction or irreversible alterations in living tissue by chemical action at the site of contact (29CFR 1917.28). Dermal corrosivity testing is conducted to identify corrosive chemicals that may cause burns and permanent scarring to the skin. Test results are used to classify and label corrosive chemicals so that consumers and workers can take appropriate precautions to prevent injury. Test results are also used to determine appropriate packaging that will minimize hazardous spills during transport. While corrosive chemicals and products have typically been identified with an *in vivo* procedure involving application of test substances to the intact skin of a rabbit, animal welfare concerns have led to the recent development and validation of *in vitro* testing methods for assessing skin corrosivity.

In 1999, the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) coordinated the independent peer review evaluation of Corrositex® (In Vitro International, Inc., Irvine, CA), an *in vitro* corrosivity testing method. ICCVAM recommendations for using Corositex® to assess dermal corrosivity were forwarded to and subsequently accepted by U.S. regulatory agencies. In 2000, a second *in vitro* method for corrosivity testing, EpiDerm (EPI-200) (MatTek Inc, Ashland, MA), was submitted to ICCVAM for consideration. ICCVAM was also notified that EpiDerm and two other *in vitro* corrosivity test methods, EPISKIN (EPISKIN SNC, Lyon, France) and the Rat Skin Transcutaneous Electrical Resistance (TER) assay, had been reviewed and endorsed by the European Centre for the Validation of Alternative Methods (ECVAM) Scientific Advisory Committee (ESAC). The ICCVAM agreed that it should evaluate all three proposed test methods.

The National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) subsequently prepared a background review document (BRD) summarizing available data, prior ECVAM validation studies, and the ESAC reviews for the three test methods. An ICCVAM Corrosivity Working Group (CWG) composed of Federal employees reviewed the BRD and concluded, based on the information provided and the outcomes of the previous reviews, that further evaluation by an independent scientific peer review panel did not appear necessary. The CWG therefore recommended that these methods undergo ICCVAM evaluation using a newly created expedited review process, and ICCVAM agreed to proceed with an expedited review. This evaluation process involved the development of a draft ICCVAM position (proposed ICCVAM test recommendations) and publication of the position in the *Federal Register* (Vol. 66, No. 189, pp.49685-6; Sept. 28, 2001) for public comment. Public comments were considered by the CWG and ICCVAM, after which the test recommendations were finalized.

ICCVAM recommends that EpiDerm, EPISKIN, and the Rat Skin TER assay can be used to assess the dermal corrosion potential of chemicals and chemical mixtures in a weight-of-evidence approach

using an integrated testing strategy for dermal irritation/corrosion. In this approach, positive *in vitro* corrosivity responses will not generally require further testing and results can be used for classification and labeling without the need for animal testing. Accordingly, these methods provide for the replacement of animal use when positive results are obtained.

As required by the ICCVAM Authorization Act of 2000 (P. L. 106-545), these ICCVAM test recommendations will be forwarded to Federal agencies for their consideration and appropriate action. Agency responses to ICCVAM test recommendations will be made available on the ICCVAM/NICEATM website (http://iccvam.niehs.nih.gov). This publication and supporting documents are also available on this website.

An added benefit realized from this review was the further development and application of the new ICCVAM expedited review process. The experience gained during this review will facilitate future ICCVAM consideration of ECVAM-validated and ESAC-endorsed methods. This process enhances the likelihood of international harmonization and provides an opportunity to develop concordant recommendations between the United States and the European Union where feasible. It also minimizes or avoids duplication of effort and avoids needless delays in achieving mutual endorsement and acceptance of scientifically valid methods.

These test method evaluations required the efforts of many individuals. We especially acknowledge the ECVAM staff who designed, managed, and analyzed the results of the independent validation studies and the efforts of the participating laboratories that conducted the validation studies. The ESAC is recognized for their careful review of the study results. Special thanks go to the NICEATM staff for preparing the Background Review Document on the test methods and for editing and publishing this final report. We appreciate the efforts of the CWG and the ICCVAM for conducting a diligent and thorough review of these three methods. Finally, we appreciate and acknowledge the reviews and comments by members of the public.

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